Medical History

William Murrell, Physician and Practical Therapist

EDITH SMITH, F. DUDLEY HART

British Medical Journal, 1971, 3, 632–633

If there is one drug that has stood the test of time it is glyceryl trinitrate in the treatment of angina pectoris. It was in 1879 that William Murrell, "Lecturer on Practical Physiology at Westminster Hospital, and Assistant-Physician to the Royal Hospital for Diseases of the Chest," first reported on its use and efficiency.[1] It is a long article, running to four successive numbers of the *Lancet*, and describes very completely the experimental work on himself and his patients with this substance. Now, 92 years later, it is still in general use, a standby and godsend to thousands of sufferers all over the world. Few, however, know anything about Murrell, and least of all the students and graduates of his own Westminster Hospital. One of us (Edith Smith) knew him personally and attended the lying-in-State of King Edward VII with him. His death on 28 June 1912 was reported in the minutes of the Westminster Hospital House Committee of 9 July that year. Few men of his day in Great Britain took a more active part in practical therapeutics. It seems a good time to lift the veil on this quiet, unassuming man, to take a good look at what he was and what he meant in the therapeutic scene of the time.

Early Years

William Murrell was born in 1853, the son of a well-known London barrister, and was educated in Wimbledon. At first interested in geology and palaeontology he later became a medical student at University College Hospital, qualifying in 1874. After a resident post at the hospital he became clinical assistant at the Brompton Hospital for Consumption; later returning to University College Hospital he won the Sharpey Scholarship in physiology and acted as demonstrator of physiology to Dr. Burdon-Sanderson. He then came under the influence of Professor Sidney Ringer, who encouraged him to take an active interest in pharmacology.

In 1877 he became a member of the Royal College of Physicians, and in the same year was appointed medical registrar and lecturer in practical physiology to the Westminster Hospital, then in Broad Sanctuary. It was from here and from the Royal Hospital for Diseases of the Chest, where he was assistant physician, that his famous work on "Nitro-glycerine as a Remedy for Angina Pectoris" appeared. It is intriguing to read this long article in his approach to the subject, his methods, his conclusions, and his literary style. He describes the previous experiments of a Mr. A. G. Field, of Brighton, who used drops of a 1% solution of nitroglycerine in alcohol by mouth. Murrell made a similar solution, and shortly before his first outpatient arrived in the clinic applied his tongue to the cork. "I had not asked my patient half a dozen questions before I experienced a violent pulsation in my head, and Mr. Field's observations rose considerably in my estimation. The pulsation rapidly increased, and soon became so severe that each beat of the heart seemed to shake my whole body. I regretted that I had not taken a more opportune moment of trying my experiments, and was afraid the patient would notice my distress, and think that I was either ill or intoxicated." Murrell observed that his pulse was full, rapid, and bounding. "The pen I was holding was violently jerked with every beat of the heart."

From that moment on he decided to make a more thorough study of the drug and took it himself 30 to 40 times, each time experiencing the same symptoms. The body temperature, he noted, was unchanged, and he roughly measured the degree of pulsation by throwing a reflected beam on to a dark wall from a mirror held in his hand. He then gave the drug to 35 subjects, 12 males and 23 females aged 12 to 58, and obtained the same general effects, noting drowsiness as an occasional side effect in his own and other cases. He made sphygmographic recordings of the effects of amyl nitrite and nitroglycerin with the assistance of Dr. Fancourt Barnes, and noted the effects of amyl nitrite to be transitory, the tracing being normal within 90 seconds of inhalation, whereas nitroglycerin took some six minutes to exert its maximal effect on the tracing, the effect being still apparent almost 30 minutes after ingestion. He does not, however, state the dose used. Finally, Murrell reported the clinical results in four patients with angina pectoris.

In this study he showed himself to be well ahead of his time in his assessment of drug action. In each case the patient was placed on placebo for a week before the trial of nitroglycerin, which was then introduced, the dose being gradually increased. All patients obtained great relief, side effects increasing as dosage was increased. Two of the four patients reported that symptoms could be aborted by taking the drug at the onset of anginal symptoms, a good example of patient co-operation. These two patients, in fact, told Murrell how to use his drug; not three or four times a day after meals, as Murrell himself initially advocated, but to abort symptoms at their first appearance. It was these two patients (Cases 1 and 3) in this small but convincing therapeutic trial who gave the drug its correct application in ischaemic heart disease. Ninety-two years later this observation still stands.

Interest in Therapeutics

Murrell from this time on became keenly interested in therapeutics and published works on massage, the treatment

Westminster Hospital, London S.W.1
EDITH SMITH, Former Matron
F. DUDLEY HART, M.D., F.R.C.P., Physician

of chronic bronchitis and gonnorrhoeal and other types of arthritis, aids to materia medica, forensic medicine, and toxicology, and the prevention of consumption. But he was once again ahead of his time, on this second occasion in his brush with authority in the use of patients in the assessment of drug action. One of us (F.D.H.) discovered this on going through the beautifully hand-written volumes of the minutes of the meeting of the Westminster Hospital House Committee. In those of 13 November 1883 the chairman, C. Hood, Esq., draws the committee's attention to an article in the *Lancet* on "Nitrite of Sodium as a Toxic Agent" by Sydney Ringer, professor of medicine at University College Hospital, and William Murrell.[2] This described the effects of this drug on frogs, cats, and Westminster Hospital outpatients. The last-named group did not like the drug at all. Out of 18 patients given the drug in doses of 10 grains 17 were unable to take it. In Murrell's own vivid words, "They said that if they ever took another dose they would expect to drop down dead, and it would serve them right." These patients experienced giddiness, throbbing headaches, faintness, nervousness, nausea, and vomiting.

The article received considerable publicity and the house committee became very concerned, for unfavourable comment had appeared in the lay press. They summoned Dr. Murrell to meet a subcommittee called to look into the matter and were concerned to find that though in the article in the *Lancet* it appeared that Professor Ringer's animal work preceded the clinical work of Dr. Murrell, in fact it was the other way round, Ringer's work on animals merely confirming the true nature of the drug as shown in the study on human subjects. They noted with relief, however, that the patients had been selected at another hospital before Murrell had been appointed assistant physician to Westminster Hospital, and they found "no grounds whatever for supposing that any patient was treated by way of simple experiment without reference to the presence of specific disease and without bona fide belief that the treatment would be beneficial to the individual patient."

They found that Dr. Murrell had been cautious in that he had used only half the dose suggested by a Dr. W. T. Law in a previous article (20 grains) and noted that no persistent ill effects had been seen in Dr. Murrell's patients, many of whom had improved on this treatment and all of whom had been willing to continue under his care. The minutes state that, "The Sub-Committee, after careful consideration of these facts, see no reason why the House Committee should withdraw from Dr. Murrell their confidence in his ability and humanity and they trust that the unfortunate manner in which the paper was put together will be forgotten while the value of his experience will remain." As a result of Murrell's work the then official dose of nitrite of sodium, 20 grains, was reduced to 2 grains, the official *B.P.* dosage today being ½-2 grains (30-120 mg).

Largely as a result of Murrell's publication and the interest it caused no fatalities were recorded with this drug in Britain until 1936, when three members of a Middlesbrough family died after ingesting it in mistake for table salt. In these days of drug trials and ethical problems in relation to them, the last paragraph of the subcommittee's report is prophetic. They recommended "that regulations be strictly enforced in respect to the treatment of outpatients, who of necessity cannot be under constant clinical observation; no remedial agent, the properties and effect of which are not fully ascertained, shall be administered by the medical officers in charge." This, be it noted, was in 1883. The problems of drug trial were there then, and Dr. Murrell narrowly missed being an early martyr on the altars of materia medica.

Personal Profile

What kind of a man was Murrell? Edith Smith remembers him well. He had a slightly brown complexion, was of medium height, neat, but never very smartly dressed. He was always polite and considerate and pleasant to the nursing staff. He commanded respect in a quiet way and expected his patients in the wards to be completely ready for his visits. His colleagues, both in Westminster and outside, respected his knowledge of poisons, and his *Aids to Materia Medica and to Forensic Medicine* and *Toxicology* and *What to do in Cases of Poisoning* were widely read. He was a bachelor, living with his sister, and did not mix very freely on social occasions. He took an active part in the Ninth International Medical Congress, being vice-president, and was also vice-president of the section on materia medica. He was elected Honorary Fellow of the Medical College of Philadelphia. Several copies of letters from his address at 38 Weymouth Street, London W.1, are in the library of the Royal College of Physicians of London. One to Dr. Ormerod, Registrar of the Royal College of Physicians, expresses deep concern that a publication under his name had appeared without his consent in the "Confectioners Union" on glucose as a food stuff.

Though a quiet, unassuming man it appears he made a few enemies, for in a letter to a friend he writes, "We have a funny custom at Westminster. When there is a vacancy on the Senior Staff, that is amongst the three Senior Physicians, the post is advertised and the man whose turn it is for promotion has to resign the appointments he holds in the Hospital and seek re-election. It is open to anyone to go against him and this time there is a fight for it. One of my colleagues was bitterly opposed to me . . . ." All appears to have gone well, however, and he was later appointed senior physician. It is of interest that he appears to have made a bigger mark in the medical world outside than inside his own hospital. He wrote many articles, mostly on therapeutic subjects, including a book on massotherapeutics in 1885, which was translated into French, German, Italian, and Russian and in which he regards massage as an accessory form of therapy and of comparatively little value in itself.

The therapy of various types of arthritis and chronic bronchitis and the prevention of consumption all occupied his attention at some time; therapeutics and applied pharmacology, forensic medicine and toxicology were throughout his main interests. He was, as a practising clinician interested primarily in therapeutics, well ahead of his time, for he sought to find out what drugs did in man and their proper place in practical therapeutics. It is to his resounding credit that his work on nitroglycerin still stands and that the drug is still in general use after so many years. It is also to his credit that sodium nitrite remains at the dosage level in the *British Pharmacopoeia* which he found correct, though almost at the expense of his appointment as consultant to Westminster Hospital.

Our thanks are due to Lord Reigate, chairman of the Board of Governors of Westminster Hospital, for permission to quote from the minutes of the house committee, to Lord Rosenheim, president of the Royal College of Physicians, for permission to quote from letters in the college library, to Mr. Payne, librarian of the college, for his kind assistance, and to the editor of the *Broadway* for permission to filch large portions of an article written in that journal by F.D.H.[3]

References

1 Murrell, W., *Lancet*, 1879, **1**, 80, 113, 151, 225.
2 Ringer, S., and Murrell, W., *Lancet*, 1883, **2**, 766.
3 Hart, F. D., *Broadway*, 1962, **R19**, 21.